DETAILED ACTION

Status of the Claims

Claims 1-13, 15-19, and 24-33 have been cancelled. Claims 14, 20-23, and 34-39 are currently pending and are the subject of this office action. This is the first office action on the merits of the claims.

Election/Restrictions

Applicants' election of Group II drawn to a method of using a selective opiate receptor modulator for prophylaxis and/or the treatment of neuropathy and related disorders and election of the following species: selective opiate receptor modulator- N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide and neuropathy related disorder-post-herpetic neuralgia, in the reply filed on 5/16/2008 are acknowledged.

Claims 23 and 34-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/16/2008.

Claims 14, 20-22, and 37-39 are under examination in the instant office action.

Information Disclosure Statement

Information Disclosure Statements have not been filed in the present application.

Priority

The instant application is a 371 of PCT/EP04/11548 filed on 10/14/2004 and claims benefit of foreign application filed on 10/30/2003. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). A certified copy of foreign application has been submitted on 4/27/2006.

The earliest effective U.S. filing date afforded the instantly claimed invention has been determined to be 10/14/2004.

Claim Rejections - 35 USC § 112 – Second paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating neuropathic pain with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide, does not reasonably provide enablement for the prophylaxis of neuropathy and related disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of using a selective opiate receptor modulator (elected species: N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide) for prophylaxis and/or the treatment of neuropathy, the clinical pictures and symptoms associated therewith, and related disorders. The instant specification fails to provide

information that would allow the skilled artisan to practice the instant invention. Attention is directed to In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. All factors have been considered together and specifically relevant factors are addressed below:

The nature of the invention. The invention is drawn to a method of using a selective opiate receptor modulator (elected species: N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide) for prophylaxis and/or the treatment of neuropathy, the clinical pictures and symptoms associated therewith, and related disorders (elected species: post-herpetic neuralgia).

The breadth of the claims: Claims 14 and 20-22 embraces prophylaxis and treatment of neuropathy and related disorders which occur by many different causes such as diabetes and virus infection. This reads on completely preventing neuropathy and related disorders. of different etiologies by administering N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide. Especially, post-herpetic neuralgia is caused by virus infection, which can not be prevented by the prophylactic treatment of N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide which is not a anti-virus agent. The specification does not enable the prophylaxis of neuropathy and related disorders

including post-herpetic neuralgia by the administration of N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide.

The state of the prior art: Neuropathy, or peripheral neuropathy, is a general term referring to disorders of peripheral nerves, usually a nerve damage as disclosed in the specification. It is studied that some opiate receptor modulators are effective for treating neuropathic pain. However, the prior art regarding preventing neuropathy and related disorders with different etiology with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide is very low or do not exist.

The predictability or unpredictability of the art: Neuropathy and related disorders are caused by diabetes, vitamin deficiency, cancer, and virus infection as disclosed in the specification. Therefore, prophylaxis of neuropathy and related disorders with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide is highly unpredictable to one skilled in the art at the time of the invention was made since it can not cure various causes of neuropathy and related disorders.

The Presence or Absence of Working Examples. Applicant does not provide any result on prophylaxis of neuropathy and related disorders with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide

The Quantity of Experimentation Needed. In light of the discussion above, Applicant would need to give examples showing results on prophylaxis of neuropathy and related disorders with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14 and 20 are rejected under 35 U.S.C. § 102(b) as being anticipated by Walker *et al*. (Pain, vol. 83, p509-516, 1999).

The instant invention is drawn to a method of prophylaxis and/or the treatment of neuropathy, the clinical pictures and symptoms associated therewith and related disorders by administrating an effective dose of a selective opiate receptor modulator (elected species: N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide), preferably N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride in an enteral or parenteral formulation to a subject in need.

Walker *et al*. teach that selective kappa-opiate agonist, asimadoline (N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride) is effective for the treatment of neuropathic pain (abstract), which is a major symptom of neuropathy as disclosed in the instant specification (p2, lines3-9). The reference further teaches intraplantar injection (a type of parental administration) into the nerve-injured paw of rat with neuropathic pain (p510, left column, 3rd paragraph and p513, left column, 2nd paragraph). As such, Walker *et al*. anticipates all the limitations of the instant claims 14 and 20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14, 20-22, and 37-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Walker *et al.* (Pain, vol. 83, p509-516, 1999) in view of Bajwa *et al.* (Geriatrics, vol. 56 (12), p18-24, 2001).

The instant invention is further drawn to a method of prophylaxis and/or the treatment of neuropathy, the clinical pictures and symptoms associated therewith and related disorders wherein the related disorders are selected from the group consisting of post-herpetic neuralgia, vulvodynia, lupus erythematosus and chemotherapy induced neuropathy (elected species: post-herpetic neuralgia) by administrating an effective dose of a selective opiate receptor modulator (elected species: N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide), preferably N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrohloride in an enteral or parenteral formulation to a subject in need.

Walker *et al.* teach that selective kappa-opiate agonist, asimadoline (N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride) is effective for the treatment of neuropathic pain (abstract), which is a major symptom of neuropathy as disclosed in the instant specification (p2, lines3-9). The reference further teaches intraplantar injection (a type of parental administration) into the nerve-injured paw of rat with

neuropathic pain (p510, left column, 3rd paragraph and p513, left column, 2nd paragraph). Walker *et al*. differs from the instant claims insofar as it does not specifically teach the treatment of post-herpetic neuralgia with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride.

Bajwa *et al*. teach that post-herpetic neuralgia is a chronic neuropathic pain syndrome that occurs as a complication of shingles, most commonly in older persons (abstract). Bajwa *et al*. further teach that combination therapy including antiviral, antidepressant, corticosteroid, opioid, and topical agents provides the most effective analgesia for post-herpetic neuralgia (abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Walker *et al.* with the teaching of Bajwa *et al.* because of the following reason: According to Walker *et al.,* asimadoline (N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride) is effective for the treatment of neuropathic pain. Bajwa *et al*. teach neurpathic pain is the symptom of post-herpetic neuralgia. Therefore, treating neuropathic pain with N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride would result in the treatment of post-herpetic neuralgia. One of ordinary skill in the art at the time the invention was made would have been motivated to use N–methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide hydrochloride for the treatment of post-herpetic neuralgia.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached on 8:00-5:00 Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Patrick J. Nolan/

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